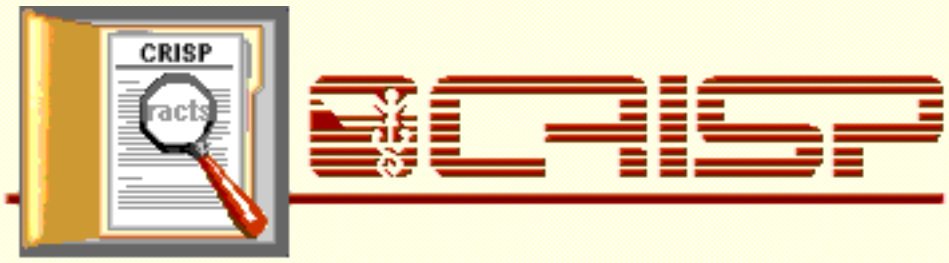
Version 2.0



Abstract

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Grant Number: 5R01NR003521-08
PI Name: HURN, PATRICIA D.
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PI Title: ASSOCIATE PROFESSOR
Project Title: ESTROGEN AS NEUROPROTECTANT IN CEREBRAL ISCHEMIA

Abstract: *Cerebral ischemia is a potentially life-threatening consequence of neurological injury in patients of both sexes. Although stroke incidence increases in women following menopause, the influence of exogenous estrogen on risk and outcomes of cerebrovascular disease in females is highly controversial. It is unclear if endogenous or exogenous estrogens mediate recovery after brain injury, or how nursing therapeutics should incorporate actual hormone status into stroke prevention/treatment plans. Using an animal model of middle cerebral artery occlusion that simulates clinical, human stroke, we have found striking neuroprotection in the female rat relative to the male when confronted with an ischemic episode. Further, the protection is eliminated by removal of endogenous estrogen but can be restored by chronic treatment with 17beta estradiol. This proposal will determine how estrogen availability is critical to brain salvage in female animals and if the benefits conferred by estrogen are important in postmenopausal females, as well as in young adults. As life expectancy increases in our population, women will soon be postmenopausal for approximately one third of their lives. Our general hypothesis is that estrogen acts via classical estrogen receptors in a trophic manner during brain injury, promoting neuronal integrity and return of function through upregulation of neurotrophic growth factors such as basic fibroblast growth factor (bFGF). The aims are to: 1) determine if acute and chronic estrogen treatment provides equivalent neuroprotection in the postmenopausal female rat (16 month) as compared to the adult, ovariectomized female (3 month); 2) determine if endogenous and exogenous estrogens produce neuroprotection via classical estrogen receptor mediated mechanisms in young and postmenopausal females; 3) distinguish the importance of estrogen receptor subtype alpha vs beta (ERalpha vs ERbeta) in estrogen's neuroprotective mechanisms and 4) determine if*

estrogen promotes stroke recovery by bFGF mediated mechanisms. Findings from this study will provide a physiological rationale for nursing care of women, both pre- and postmenopausal, who sustain brain injury from stroke, circulatory arrest or invasive neurosurgical procedures.

Thesaurus Terms:
brain disorder chemotherapy, cardiovascular disorder chemotherapy, cerebral ischemia /hypoxia, estrogen, estrogen receptor, neuroprotectant, nonhuman therapy evaluation, receptor expression, stroke
brain circulation, cerebral circulation, cerebral cortex, corpus striatum, estradiol, fibroblast growth factor, postmenopause
behavior test, female, immunocytochemistry, laboratory rat, mature animal, ovariectomy, western blotting

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